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10/621,803	07/17/2003	Kenneth A. Browne	GP131-03.UT	5941

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EXAMINER	
STRZELECKA, TERESA E	

ART UNIT	PAPER NUMBER
1637	

NOTIFICATION DATE	DELIVERY MODE
02/26/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/621,803	BROWNE, KENNETH A.	
	Examiner	Art Unit	
	TERESA E. STRZELECKA	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 May 2007 and 19 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44-52 and 54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44-52 and 54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/2/07;11/19/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This office action is in response to an amendment filed May 2, 2007 and November 19, 2007. Claims 44-53 were previously pending. Applicant amended claim 44, cancelled claim 53 and added new claim 54. Claims 44-52 and 54 are pending and will be examined.

2. Applicant's amendments overcame all of the previously presented rejections.

3. This office action contains new grounds for rejection necessitated by amendment.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 44-48 and 50-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adams et al. (U.S. patent No. 6,060,288 A; cited in the previous office action), Hanninen et al. (U. S. Patent No. 6,310,354 B1; cited in the previous office action) and Mueller et al. (Histochem. Cell Biol., vol. 108, pp. 431–437, 1997; cited in the previous office action).

A) Regarding claim 44, Adams et al. teach a device for detecting a target nucleic acid, the device comprising:

a solid support bead having a surface (Adams et al. teach a device for amplifying nucleic acids comprising beads (Fig. 1; col. 6, lines 65-67; col. 7, lines 41, 42).);

an amplification primer immobilized to the surface of said solid support bead, said amplification primer comprising a promoter sequence for an RNA polymerase and a sequence complementary to a first strand of said target nucleic acid (Adams et al. teach an amplification

primer immobilized to the beads, the primer being complementary to a target nucleic acid (Fig. 1; col. 2, lines 4-25; col. 3, lines 41-62).; and

a labeled hybridization probe separate from the amplification primer immobilized to said surface,

wherein said labeled hybridization probe comprises a sequence complementary to an amplicon synthesized using said amplification primer and said target nucleic acid as a template in a nucleic acid amplification reaction, and

wherein prior to contact of said device with any nucleotide polymerizing enzyme said labeled hybridization probe comprises a detectable label and is immobilized to said surface (Adams et al. teach detection of the amplicons with labeled hybridization probes (col. 4, lines 57-67); col. 13, lines 8-16). Therefore, since the probe is hybridized to an immobilized amplicon, the probe is itself immobilized, according to Applicant's definition. The probe is labeled independently of the polymerization reaction being performed.).

Regarding claim 45, Adams et al. teach glass and plastic (col. 7, lines 45-51; col. 14, lines 36-44).

Regarding claims 46-48, Adams et al. teach covalent immobilization of primers (col. 2, lines 1-3).

Regarding claim 50, Adams et al. teach multiplex detection of different targets using primers with different sequences (col. 5, lines 3-13).

Regarding claims 51 and 52, Adams et al. teach immobilization of a single primer on the solid support (col. 2, lines 1-63; col. 5, lines 7-9; col. 22, lines 48-56; col. 23, lines 19-26).

B) Adams et al. probes binding to an immobilized amplicon, but do not teach immobilized labeled probes.

C) Hanninen et al. teach a method of detection of PCR amplification using different combinations of immobilized primers and/or primers and probe, and they teach immobilized labeled fluorescent probes (col. 4, lines 23-33, 39-63; col. 5, lines 5-10 and 35-41; col. 6, lines 59-67; col. 7, lines 1-5).

Therefore it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used immobilized labeled probe of Hanninen et al. in the method of amplification detection of Adams et al. with a reasonable expectation of success. The motivation to do so is provided by Adams et al., who stated (col. 3, lines 41-62):

"In another embodiment of the present invention, a pair of oligonucleotides is immobilized on the solid support. For example, a pair of oligonucleotide primers (e.g., primer (a) and primer (b)) can be used, with the nucleotide sequence of each primer complementary to a different region of the target nucleic acid sequence. Typically the different regions of the target sequence are at opposite ends of the target sequence. During the annealing step of the amplification reaction, a single-stranded target nucleic acid molecule, which has been formed by the elongation of primer (a), comprises a region of sequence (b) at the opposite end of the strand. Because this single-stranded target sequence is still immobilized on the solid support, and if a second primer is present on the solid support with a sequence complementary to sequence (b), the end of this target sequence will anneal to primer b, and a target molecule will form that is attached to the solid support at both ends. This molecule essentially forms a "bridge" between primer (a) and primer (b). Thus, multiple target sequences can be readily detected simultaneously

because the amplification products are "captured" on the support and cannot dissociate back into solution and possibly escape detection."

Therefore, since the second primer of Adams is really an unlabeled probe to which the amplified first strand binds, having a labeled probe in the vicinity of the amplification primer would allow instant detection of the amplified fragment, since it would bind to the probe, rather than dissociating into solution.

D) Adams et al. teach amplification of RNA targets (col. 8, lines 3-5), but do not specifically teach amplification using primers comprising a promoter for RNA polymerase, T7 RNA polymerase or reverse transcriptase.

E) Mueller et al. teach amplification of RNA targets using a self-sustained sequence replication method (3SR), which uses a primer containing a T7 polymerase promoter, T7 RNA polymerase and AMV reverse transcriptase (Fig. 1; page 432, third paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art to have used the 3SR reagents of Mueller et al. in the device of Adams et al. and Hanninen et al. with a reasonable expectation of success. The motivation to do, provided by Mueller et al., would have been, as stated on page 432, last paragraph and page 433, first and second paragraphs:

"Despite its complexity at the molecular level, the 3SR reaction is simple to perform since all enzymes can be added in a single step to a single reaction mixture at a constant temperature. There is no need for a thermocycler or for heat stable enzymes and, since there are no denaturing conditions, there is no need to add fresh enzymes. (For additional comments comparing PCR to 3SR see Lown 1993.)

Regarding reaction kinetics, the rate of amplification with 3SR is extremely fast in comparison to PCR, especially in the early phases of the reaction. HIV viral RNA has been found to multiply 12 copies to 1010 copies in 90 min by in vitro 3SR (Bush et al. 1992). Another study showed that, while PCR required 85 min to amplify a template 105 times, 3SR can reach the same level of amplification in 15 min (Guatelli et al. 1990). This rapid rate of amplification means that the incubation time for the 3SR reaction can be quite short, usually only 1–2 h."

6. Claim 49 is rejected under 35 U.S.C. 103(a) as being unpatentable over Adams et al. (U.S. patent No. 6,060,288 A; cited in the previous office action), Hanninen et al. (U. S. Patent No. 6,310,354 B1; cited in the previous office action) and Mueller et al. (Histochem. Cell Biol., vol. 108, pp. 431–437, 1997; cited in the previous office action), as applied to claim 44 above, and further in view of Fang et al. (J. Am. Chem. Soc., vol. 121, pp. 2921-2922, 1999; cited in the IDS).

A) The teachings of Adams et al., Hanninen et al. and Mueller et al. are presented above. Regarding claim 49, Hanninen et al. teach fluorescently labeled probes, but do not teach probes comprising fluorophore and a quencher.

B) Regarding claim 49, Fang et al. teach detection of nucleic acid targets using molecular beacons immobilized to a solid surface (page 2922, paragraphs 2 and 4-6).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used the molecular beacons of Fang et al. as the fluorescent probes in the method of Adams et al., Hanninen et al. and Mueller et al. with a reasonable expectation of success. The motivation to do so, provided by Fang et al., would have been, as stated by Fang et al. (page 2921, first paragraph and page 2922, fifth paragraph):

"MBs have extremely high selectivity with single base pair mismatch identification capability. They hold great promise for studies in genetics, disease mechanisms, and molecular interactions, for applications in disease diagnostics, and in new drug development."

"Our results indicate the MB-immobilized plate can be used to detect target DNA molecules in the subnanomolar range. In addition, preliminary experiments have shown that the immobilized DNA molecules on the plate can be regenerated after hybridization. Therefore, we will be able to reuse the plate multiple times for DNA detection and interaction studies."

7. Claim 54 is rejected under 35 U.S.C. 103(a) as being unpatentable over Adams et al. (U.S. patent No. 6,060,288 A; cited in the previous office action), Hanninen et al. (U. S. Patent No. 6,310,354 B1; cited in the previous office action) and Mueller et al. (Histochem. Cell Biol., vol. 108, pp. 431–437, 1997; cited in the previous office action), as applied to claim 44 above, and further in view of Majlessi et al. (Nucl. Acids Res., vol. 26, pp. 2224-2229, 1998; cited in the IDS).

A) The teachings of Adams et al., Hanninen et al. and Mueller et al. are presented above. They do not teach probes comprising 2'-methoxy nucleotide analogs.

B) Majlessi et al. teach probes comprising 2'-methoxy nucleotide analogs (Abstract) and their use in detection of RNA targets (page 2228, last two paragraphs; page 2229; Fig. 3).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used the 2'-methoxy nucleotide analogs of Majlessi et al. as the fluorescent probes in the method of Adams et al., Hanninen et al. and Mueller et al. with a reasonable expectation of success. The motivation to do so, provided by Majlessi et al., would have been, as stated by Majlessi et al. (page 2229, last paragraph):

"In summary, 2'-*O*-methyl oligoribonucleotide probes afford multiple advantages over 2'-deoxy oligoribonucleotide probes for detecting RNA targets, including greatly increased *T*m, which allows use of shorter probes, faster kinetics of hybridization, ability to bind to structured targets under conditions where 2'-deoxy oligoribonucleotide probes will not and significantly improved specificity. These advantages render 2'-*O*-methyl oligoribonucleotide probes superior to 2'-deoxy oligoribonucleotide probes for use in assays that detect RNA targets."

8. No claims are allowed.

Conclusion

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TERESA E. STRZELECKA whose telephone number is (571)272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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February 15, 2008